

ROBUST SUMMARIES

201-14995B

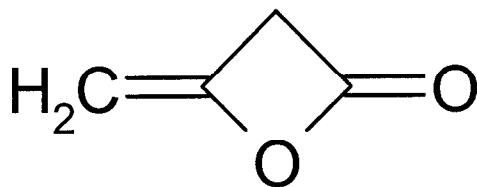
I. General Information

CAS Number: 674-82-8

Name: 4-Methylene-2-oxetanone
Acetyl ketene
Diketene
But-3-en-3-olide

Formula : $C_4H_4O_2$

Structure:



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II. Physical-Chemical Data

A. Melting Point

| | |
|--|--|
| Test Substance Test Substance: Remarks: | Diketene Purity: Not specified |
| Method Method: GLP: Year: | Not specified Unknown 1979 |
| Results Melting Point value: | - 6.5°C |
| Reference | Sax, N.I., Dangerous Properties of Industrial Materials, 5 th ed., New York, Van Nostran Rhienhold, 1979. |
| Test Substance Test Substance: Remarks: | Diketene Purity: Not specified |
| Method Method: GLP: Year: | Not specified Unknown 1990 |
| Results Melting Point value: | - 7.5°C |
| Reference | Elvers, B. et al, ed., Ullmann's Encyclopedia of Industrial Chemistry, Completely Revised 5th ed., New York, VCH Publishers, 1990. |

B. Boiling Point

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|--|--|
| Test Substance Test Substance: Remarks: | Diketene Purity: Not specified |
| Method Method: GLP: Year: | Not specified Unknown 1994 |
| Results Boiling Point value: | 127.4 °C |
| Reference | Sax, N.I., Dangerous Properties of Industrial Materials, 8 th ed., New York, Van Nostran Rhenhold, 1994. |
| Test Substance Test Substance: Remarks: | Diketene Purity: Not specified |
| Method Method: GLP: Year: Remarks: | Not specified Unknown 1990 |
| Results Boiling Point value: Pressure with units: Decomposition: Remarks: | 127.4 °C 101.3 kPa 350 – 600 °C |
| Reference | Elvers, B. et al, ed., Ullmann's Encyclopedia of Industrial Chemistry, Completely Revised 5th ed., New York, VCH Publishers, 1990. |

C. Vapor Pressure

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|--|---|
| Test Substance Test Substance: Remarks: | Diketene Purity: Not specified |
| Method Method: GLP: Year: | Not specified Unknown 1989 |
| Results Vapor pressure value: Temperatures: | 10.7 mm Hg 25 °C |
| Reference | Daubert, T.E. & R.P. Danner, Physical and Thermodynamic Properties of Pure Chemicals: Data Compilation, Design institute for Physical Properties Data, Amer. Inst. Chem. Eng., Hemisphere Pub. Corp., New York, NY, 4 Vol., 1989. |
| Test Substance Test Substance: Remarks: | Diketene Purity: Not specified |
| Method Method: GLP: Year: | Not specified Unknown 1990 |
| Results Vapor pressure value: Temperatures: | 1.07 kPa 20 °C |
| Reference | Elvers, B. et al, ed., Ullmann's,encyclopedia of Industrial Chemistry, Completely Revised 5th ed., New York, VCH Publishers, 1990. |

D. Partition Coefficient

| | |
|---|--|
| Test Substance Test Substance: | Diketene |
| Method Method: | Estimation |
| Results Log P _{ow} : Remarks: | - 0.39 |
| Reference | KOWIN (v1.67); EPI SUITE™ (v3.11) Meylan, W.M. and P.H. Howard. 1995. Atom/fragment contribution method for estimating octanol-water partition coefficients. <i>J. Pharm. Sci.</i> 84 :83-92. |

E. Water Solubility

| | |
|--|--|
| Test Substance Test Substance: | Diketene |
| Method Method: | Estimation |
| Results Value: Temperature: | 5.30 E+005 mg/l (530 g/l) 25°C |
| Reference | WSKOWWIN (v1.41); EPI SUITE™ (v3.11) Meylan, W.M., P.H. Howard, R.S. Boethling. 1996. Improved method for estimating water solubility from octanol/water partition coefficient. <i>Environ. Toxicol. Chem.</i> 15 :100-106. |
| Test Substance Test Substance: Remarks: | Diketene Purity unknown |
| Method Method: | Unknown |
| Results Value: Remarks: | Soluble Decomposes in water |
| Reference | Sax, N.I., Dangerous Properties of Industrial Materials, 8 th ed., New York, Van Nostran Rhenhold, 1994. |

III. Environmental Fate Endpoint

A. Photodegradation

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|---|---|
| Test Substance Test Substance: Remarks: | Diketene |
| Method Method: Test type: | Estimation Atmospheric Oxidation |
| Results Temperature: Hydroxyl radical reaction OH Rate constant: Half-life: Ozone reaction: Ozone Rate constant: Half-life: Remarks: | 25 °C 5.15 x 10E-11 cm ³ /molecule-sec 0.208 days (12-hr/day; 1.5 x 10E6 OH/cm ³) 1.14 x 10E-17 cm ³ /molecule-sec 1.0 days at 7 x 10E11 O ₃ /cm ³ Estimated value based upon acceptable model |
| Conclusions | Material is oxidized by atmospheric hydroxyl radicals at a rapid rate and by Ozone at a moderate rate. |
| Reference | AOPWIN (v1.91); EPI SUITE™ (v3.11); Meylan, W.M. and P.H. Howard (1993), Computer estimation of the atmospheric gas-phase reaction rate of organic compounds with hydroxyl radicals and ozone. <i>Chemosphere</i> 26 :2293-2299. |

B. Stability in Water

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|---|---|
| Test Substance Test Substance: Remarks: Method Method: Test type: GLP: Year: Results Nominal value: Remarks: Conclusions Reference | Diketene Purity unknown Experimental Kinetic measurement – Heat of Reaction Unknown 1992 $\Delta_r H^\circ = -118.5 \text{ kJ/mol}$ liquid phase; solvent:solution The material is predicted to readily undergo hydrolysis. E.B. Lopatin, <i>et al.</i> , <i>Kinetic and thermochemical characteristics of diketene-based reactions</i> , Khim.-Farm. Zh., 1992; 26 : 76-78. |
| Test Substance Test Substance: Remarks: Method Method: Test type: GLP: Year: Results Nominal value: Remarks: Conclusions Reference | Diketene Purity unknown Experimental Automatic Recording pH Titration No 1966 Hydrolysis Rate Constant, $k = 120 \text{ min}^{-1} \times 10^3$ (25°C) liquid phase; automatic addition of standardized base via capillary burette with instrument set to maintain constant pH of 7.0. Diketene, which is the anhydride of acetoacetic acid, was determined to hydrolyze extremely rapidly in water. B. L. Van Duuren and B.M. Goldschmidt., <i>Carcinogenicity of Epoxides, Lactones and Peroxy Compounds. III. Biological and Chemical Reactivity</i> , J Med Chem, 1966; 9 : 77-79. |

C. Biodegradation

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|---|--|
| Test Substance Test Substance: Remarks: | Diketene Purity unknown |
| Method Method: Test type: GLP: Year: Contact time: Inoculum: Remarks: | Modified MITI Test, OECD: TG-301C Ready biodegradability: Modified MITI Test (I) Yes 1992 28 days Activated sludge 300ml of test solution with a concentration of 100 mg/l of test substance was cultivated at 25°C for 28 days with a concentration of 30 mg/l of activated sludge. |
| Results Results: Degradation %: Time for 10% degradation: Classification: Breakdown products: Remarks: | 95-102% Not noted Material determined to be readily biodegradable under the definition of the test. Not determined |
| Conclusions | Results indicate material would not be persistent in the environment. |
| Reference | Chemicals Inspection and Testing Institute; Biodegradation and Bioaccumulation Data of Existing Chemicals Based on the CSCL Japan; Japan Chemical Industry Ecology – Toxicology and Information Center, ISBN 4-89074-101-1; 1992. |

D. Transport between Environmental Compartments (Fugacity)

| Test Substance Test substance: Remarks: | Diketene | | | | | | | | | | |
|--|---|--|------------------|-----|------|-------|------|------|------|----------|-------|
| Method Test type: Model used: Remarks: | Estimation Level III Fugacity Model; EPIWIN:EQC from Syracuse Research Corporation Physical chemical values utilized in this model were -7.0 °C for MP, 127.4 °C for BP, and 10.7 mmHg for VP | | | | | | | | | | |
| Results Model data and results: Estimated distribution and media concentration (levels II/III): | <table><tr><th></th><th>Distribution (%)</th></tr><tr><td>Air</td><td>3.65</td></tr><tr><td>Water</td><td>68.7</td></tr><tr><td>Soil</td><td>27.6</td></tr><tr><td>Sediment</td><td>0.115</td></tr></table> | | Distribution (%) | Air | 3.65 | Water | 68.7 | Soil | 27.6 | Sediment | 0.115 |
| | Distribution (%) | | | | | | | | | | |
| Air | 3.65 | | | | | | | | | | |
| Water | 68.7 | | | | | | | | | | |
| Soil | 27.6 | | | | | | | | | | |
| Sediment | 0.115 | | | | | | | | | | |
| Reference | Meylan, W. (1993). User's Guide for the Estimation Programs Interface (EPIWIN v 3.11) Syracuse Research Corporation, Syracuse, New York 13210. The Level III model incorporated into EPIWIN is a Syracuse Research Corporation adaptation of the methodology described by Mackay <i>et al.</i> 1996; <i>Environ. Toxicol. Chem.</i> 15(9) , 1618-1626 and <i>Environ. Toxicol. Chem.</i> 15(9) , 1627-1637. | | | | | | | | | | |

IV. Ecotoxicity

A. Acute Toxicity to Fish

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| Test Substance Test Substance: Remarks: | Diketene Purity unknown |
| Method Method: Test type: GLP: Year: Species/strain: Analytical monitoring: Exposure duration: Remarks: | Other Acute toxicity to fish No (pre-GLP) 1978 Golden Orfe (<i>Leucius idus melanotus</i>) Not listed Not listed |
| Results Endpoint values: | $LC_{50} = 150 \text{ mg/L}$ |
| Data Quality Reliability: Remarks: | Not assignable |
| Reference | L. Goetsching et al., Pap.-Eucepa Symp., 1978, 389-408 |
| Test Substance Test Substance: | Acetoacetic acid |
| Method Method: Test type: GLP: Year: Species/strain: Exposure duration: Remarks: | Other: model calculation Acute toxicity to fish No 2003 Fish/unknown 96 hours Model compound class is neutral organics – acid. Physical-chemical inputs were default values. |
| Results Endpoint values: | $EC_{50} = 479,000 \text{ mg/L}$ |
| Data Quality Reliability: Remarks: | Reliable with restriction Modeled data |
| Reference | ECOSAR Program (v0.99); EPIWIN (v3.11) |

B. Acute Toxicity to Aquatic Invertebrates

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| Test Substance Test Substance: | Acetoacetic acid |
| Method Method: Test type: GLP: Year: Species/strain: Exposure duration: Remarks: | Other: model calculation Acute toxicity to Daphnid No 2003 Daphnid 48 hours Model compound class is neutral organics – acid. Physical-chemical inputs were default values. |
| Results Endpoint values: | EC ₅₀ = 418,000 mg/L |
| Data Quality Reliability: Remarks: | Reliable with restriction Modeled data |
| Reference | ECOSAR Program (v0.99); EPIWIN (v3.11) |

C. Toxicity to Aquatic Plants

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|--|--|
| Test Substance Test Substance: | Acetoacetic acid |
| Method Method: Test type: GLP: Year: Species/strain: Exposure duration: Remarks: | Other: model calculation Biomass No 2003 Green algae 96 hours Model compound class is neutral organics – acid. Physical-chemical inputs were default values. |
| Results Endpoint values: | EC ₅₀ = 220,000 mg/L |
| Data Quality Reliability: Remarks: | Reliable with restriction Modeled data |
| Reference | ECOSAR Program (v0.99); EPIWIN (v3.11) |

V. Toxicological Data

A. Acute Toxicity

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|--|---|
| Test Substance Test Substance: Remarks: Method Method: Test type: GLP: Year: Species/strain: Sex: Animal/sex/dose: Vehicle: Route of exposure: Remarks: Results Value: Deaths at each dose level: Proper statistical evaluation used: Remarks: Conclusions Data Quality Reliability: Remarks: References: | Ketene dimer Purity unknown Other Acute oral toxicity No (preGLP) 1974 Rat/Carworth-Wistar Male 5 None indicated. Oral (gavage) Specific dose levels not listed LD50 = 0.56 ml/kg Not indicated Yes, Thompson and Weil Reliable with restrictions Significant amounts of study detail not published C. Carpenter <i>et al.</i> , Toxicol. Appl. Pharmacol., 28 , 313-319, 1974. |
| Test Substance Test Substance: Remarks: Method Method: Test type: GLP: Year: Species/strain: Sex: Animals/Dose: Vehicle: Route of exposure: Remarks: Results Value: Deaths at each dose level: Proper statistical evaluation used: Remarks: | Diketene Purity unknown Other Acute toxicity No (preGLP) 1961 Rat / unknown strain Unknown 10 animals; Dose range 100 - 1600 mg/kg Corn oil Oral gavage Study lasted 14 days LD ₅₀ = 400 – 800 mg/kg Unknown, deaths occurred between 4.5 hrs to 11 days Unknown Rats were noted to be normal to very weak, rough coat, sides caved in, cyanosis, labored respiration, prostration |

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| <p>Conclusions</p> <p>Data Quality Reliability: Remarks:</p> <p>References:</p> | <p>Reliable with restrictions Significant amounts of study detail not published</p> <p>Laboratory of Industrial Medicine; Eastman Kodak Company; Rochester, NY; November 22, 1961.</p> |
| <p>Test Substance Test Substance: Remarks:</p> <p>Method Method: Test type: GLP: Year: Species/strain: Sex: Animals/dose: Vehicle: Route of exposure: Remarks:</p> <p>Results Value: Deaths at each dose level: Proper statistical evaluation used:</p> <p>Remarks:</p> <p>Conclusions</p> <p>Data Quality Reliability: Remarks:</p> <p>References:</p> | <p>Diketene Purity unknown</p> <p>Other Acute toxicity No (preGLP) 1961 Mouse / unknown strain Unknown 20 animals; Dose range 100 - 3200 mg/kg Corn oil Oral gavage Study lasted 14-days</p> <p>LD50 = 800 - 1600 mg/kg Unknown, deaths occurred between 0.75 to 1 day Unknown</p> <p>Mice were noted to be normal to very weak, rough coat, sides caved in, diarrhea in high doses, tremor prostration</p> <p>Reliable with restrictions Significant amounts of study detail not published</p> <p>Laboratory of Industrial Medicine; Eastman Kodak Company; Rochester, NY; November 22, 1961.</p> |
| <p>Test Substance Test Substance: Remarks:</p> <p>Method Method:</p> <p>Test type: GLP: Year: Species/strain: Sex: Animal/sex/dose:</p> | <p>Diketene Purity unknown</p> <p>Other: NAS-NRC - Principles and Procedures for Evaluating the Toxicity of Household Substances, Pub 1138, 1964. Acute oral toxicity No (preGLP) 1967 Rat Unknown Unknown</p> |

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| Vehicle: Route of exposure: Remarks: Results Value: Deaths at each dose level: Proper statistical evaluation used: Remarks: Conclusions Data Quality Reliability: Remarks: References: | None indicated Oral Specific dose levels not listed LD ₅₀ = 0.54 g/kg Not indicated. Unknown Reliable with restrictions Significant amounts of study detail not published W.E. Rhinehart <i>et al.</i> , Indust. Hyg, Found. Of Amer., Chemical and Toxicological Series, Bulletin, 6, 1-11, 1967. |
| Test Substance Test Substance: Remarks: Method Method: Test type: GLP: Year: Species/strain: Sex: Animal/sex/dose: Vehicle: Route of exposure: Remarks: Results Value: Deaths at each dose level: Proper statistical evaluation used: Remarks: Conclusions Data Quality Reliability: Remarks: References: | Diketene Purity: Unknown Other Acute dermal toxicity No 1967 Rabbit Not listed. Not listed None indicated Dermal LD ₅₀ = 6.73 g/kg Not indicated. Yes Reliable with restrictions Significant amounts of study detail not published W.E. Rhinehart et al, Indust. Hyg, Found. Of Amer., Chemical and Toxicological Series, Bulletin, 6, 1-11, 1967. |

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| <p>Test Substance Test Substance: Remarks:</p> <p>Method Method: Test type: GLP: Year: Species/strain: Sex: Animal/sex/dose: Vehicle: Route of exposure: Remarks:</p> <p>Results Value: Deaths at each dose level: Proper statistical evaluation used: Remarks:</p> <p>Conclusions</p> <p>Data Quality Reliability: Remarks:</p> <p>References:</p> | <p>Ketene dimer Purity unknown</p> <p>Other Acute dermal toxicity No 1974 Rabbit Not listed Not listed None indicated. Dermal</p> <p>LD50 = 2.83 ml/kg Unknown Yes, Thompson and Weil</p> <p>Reliable with restrictions Significant amounts of study detail not published</p> <p>C. Carpenter et al., Toxicol. Appl. Pharmacol., 28, 313-319, 1974.</p> |
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| <p>Test Substance Test Substance: Remarks:</p> <p>Method Method: Test type: GLP: Year: Species/strain: Sex: Animal/sex/dose: Route of exposure: Remarks:</p> <p>Results Value: Deaths at each dose level: Remarks: Proper statistical evaluation used:</p> <p>Conclusions</p> <p>Data Quality Reliability: Remarks:</p> <p>References:</p> | <p>Diketene Purity unknown</p> <p>Other Acute toxicity Yes 1987 Rat / COBS CD(SD)BR Male and Female 5/sex/dose; vapor concentration range 250, 500, 750 ppm Inhalation; 1 hour Study lasted 14-days and evaluated toxicity after 1 hour of exposure to diketene in vapor form. Vapors were generated by metering test material into a heated glass bead column. Animals were exposed in a 420L stainless steel and glass inhalation chamber. Temperature and relative humidity were 69-73 °F and 56-65% respectively. Animals were monitored for 14 days post exposure. Animals (approx. 8 weeks old) weighed 201-214 g (males) and 210-234 (females) at study initiation</p> <p>LD₁₀ = 346 ppm (males); 410 ppm (females); 370 ppm (both sexes) Deaths were seen at 250 ppm in either sex. At 500 ppm, two males and one female died on Day 1. At 750 ppm one male and two females died on Day 1. On Day 2, two males and one female died. One of each sex died on Day 6. Weight gains were initially slow until Day 7 but ultimately all dose groups had positive gains at termination. Clinical signs of respiratory, eye irritation, and dyspnea were noted at all levels. No compound-related gross pathology was seen in animals found dead or in those surviving until Day 14. Probit analysis</p> <p>Reliable without restrictions This was a well-documented study conducted under GLP assurances</p> <p>Acute inhalation toxicity and one-hour LC10 value of diketene in the rat. Health and Environmental Laboratories; Eastman Kodak Company; Rochester, NY; HAEL No.: 85-0085; February 4, 1987.</p> |
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B. Repeated Dose Toxicity

Please refer to data submitted to the US EPA HPV program on methyl acetoacetate (CAS No.: 105-45-3) and to data submitted to the US EPA as part of the OECD SIDS program on ethyl acetoacetate (CAS No.: 141-97-9).

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|--|--|
| Test Substance Test Substance: Remarks: | Diketene Purity: Not listed |
| Method Method: Test type: GLP: Year: Species/strain: Route of exposure: Duration of test: Dose level(s): Sex: Control group & treatment: Post-exposure observation period: Remarks: | Other Life-time dermal carcinogenicity study No 1967 mouse/Swiss 3 X weekly Dermal application 493/529-days 100 mg of 10% solution diketene in acetone and tricaprylin Female 30 mice Not listed |
| Results NOAEL: Toxic responses by dose: Proper statistical evaluation used: Remarks: | 100 mg of 10% solution Observations: Substance found to be inactive, no excess Tumors observed. Yes |
| Conclusions | Material not found to be carcinogenic by dermal application in mice. |
| Data Quality Reliability: Remarks: | Reliable with restriction. |
| References: | B.L. van Duuren, <i>et al.</i> , Nat. Cancer Inst. 39 , 1217-1228, 1967. |
| Test Substance Test Substance: Remarks: | Diketene Purity: Not listed |
| Method Method: Test type: GLP: Year: Species/strain: Route of exposure: Duration of test: Dose level(s): Sex: | Other Life-time subcutaneous carcinogenicity study No 1967 Rat/Sprague-Dawley 1 X weekly Subcutaneous injection 543-days 4 mg Not listed |

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|--|---|
| Control group & treatment: Post-exposure observation period: Remarks: Results NOAEL: Toxic responses by dose: Proper statistical evaluation used: Remarks: Conclusions Data Quality Reliability: Remarks: References: | Not listed Not listed 4 mg Observations: Substance found to be inactive, no sarcomas observed. Yes Material not found to be carcinogenic by subcutaneous application in mice. Reliable with restriction. B.L. van Duuren, <i>et al.</i> , Nat. Cancer Inst. 39, 1213-1216, 1967. |
| Test Substance Test Substance: Remarks: Method Method: Test type: GLP: Year: Species/strain: Route of exposure: Duration of test: Dose level(s): Sex: Control group & treatment: Post-exposure observation period: Remarks: Results NOAEL: Toxic responses by dose: Proper statistical evaluation used: Remarks: Conclusions Data Quality Reliability: Remarks: | Diketene Purity: Not listed Other Subcutaneous implantation carcinogenicity study No 1969 Rat/Sprague-Dawley Single subcutaneous implantation of gelatin capsule 20-months 1.1 mg Diketene in 10 mg of trilaurin-tricaprylin (4:1) 40 Female Not listed. Capsule implantation made in left axillary region. Not listed Purpose of capsule implantation was to allow for slow seepage of the Diketene into the surrounding tissue. 1.1 mg Diketene in 10 mg of trilaurin-tricaprylin (4:1) Observations: Substance found to be inactive, no local tumors observed. Yes No tumors were seen at site of implantation. Material was not found to be carcinogenic by subcutaneous implantation in rats. Reliable with restriction. |

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| References: | B.L. van Duuren., Carcinogenic epoxides, Lactones and Halo-ethers and their Mode of Action, Ann NY Acad Sci, 1969; 163 :633-651. |
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C. Genetic Toxicity – Mutation

Please refer to data submitted to the US EPA HPV program on methyl acetoacetate (CAS No.: 105-45-3) and to data submitted to the US EPA as part of the OECD SIDS program on ethyl acetoacetate (CAS No.: 141-97-9).

D. Genetic Toxicity – Chromosomal Aberrations

Please refer to data submitted to the US EPA HPV program on methyl acetoacetate (CAS No.: 105-45-3) and to data submitted to the US EPA as part of the OECD SIDS program on ethyl acetoacetate (CAS No.: 141-97-9).

E. Developmental Toxicity

Please refer to data submitted to the US EPA HPV program on methyl acetoacetate (CAS No.: 105-45-3) and to data submitted to the US EPA as part of the OECD SIDS program on ethyl acetoacetate (CAS No.: 141-97-9).

F. Reproductive Toxicity

Please refer to data submitted to the US EPA HPV program on methyl acetoacetate (CAS No.: 105-45-3) and to data submitted to the US EPA as part of the OECD SIDS program on ethyl acetoacetate (CAS No.: 141-97-9).